PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

MAJEED et al. Attorney Dkt. No.: 108064-00051

Appln. No.: National Stage Application based on PCT/US01/41748

Filed: Concurrently herewith

For: BIOAVAILABLE COMPOSITION OF NATURAL AND SYNTHETIC HCA

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231 December 11, 2001

Sir:

Prior to initial examination of the application, please amend the above-identified application as follows:

IN THE SPECIFICATION:

Please amend the specification as follows. A marked-up copy of the original specification showing the changes is attached.

Page 1, lines 7 and 8 should read as follows:

--CROSS-REFERENCE TO RELATED APPLICATION

This application is a National Stage entry of International Application No. PCT/US01/41748, filed on August 17, 2001, which claims priority under 35 USC §1.119(e) to provisional Application Serial No. 60/225,821, filed on August 17, 2000, the entire specification, claims and drawings of which are incorporated herewith by reference. --

REMARKS

In the event that any fees are due with respect to the filing of this paper, please charge Deposit Account No. 01-2300, referencing Attorney Docket No. 108064-00051.

Respectfully submitted,

Lynn A. Bristol
Registration No. 48,898

ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W.,
Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000
Fax: (202) 638-4810

LAB/ccd

Marked up copy of specification

Bioavailable Composition of Natural and Synthetic HCA

CROSS REFERENCE TO RELATED APPLICATION

This application is a National Stage Entry of International Application No. PCT/US01/41748, filed on August 17, 2001. This application claims priority under 35 U.S.C. §1.119(e) to provisional application serial no. 60/225,821, filed on August 17, 2000. The entire specification, claims and drawings of which are incorporated herewith by reference.

Background of the invention

Hydroxycitric acid is an alpha-hydroxy tribasic acid (1,2-dihydroxypropane-1,2,3-tricarboxylic acid) with two asymmetric centers, hence the formation of two pairs of diasteroisomers or four different isomers: (-)hydroxycitric acid (I), (+)hydroxycitric acid (II), (-)allo-hydroxycitric acid (III), and (+)allo-hydroxycitric acid (IV). (1-2) The (-)hydroxycitric acid (HCA) isomer is found in the rind of Garcinia cambogia fruit (fam. Clusiaceae). (1-2) This isomer has been shown to be a potent linear competitive inhibitor of ATP citrate lyase enzyme, in vitro, demonstrating a much greater affinity for the purified enzyme than its natural substrate citrate as well as the other stereoisomers of hydroxycitric acid. (1-2) The biological importance of ATP citrate lyase is as a citrate cleavage enzyme which catalyzes the extramitochondrial cleavage of citrate to acetyl CoA and oxaloacetate, and facilitates the biosynthesis of fatty acids. The reversible inhibition of citrate lyase by (-) HCA may lead to the reduction of fatty acids synthesis and lipogenesis. These effects have been measured and demonstrated in vivo following the oral, intravenous or intraperitoneal administration of (-)hydroxycitrate to experimental animals. (3) When (-) HCA was given orally before the feeding period, the animals fed (-) HCA consumed less food and their hepatic synthesis of fatty acids and cholesterol was significantly diminished as compared to the untreated controls. (3-4) The observed decrease in food intake may be only one of the factors responsible for the (-) HCA promoted weight loss, because experimentation with rats fed (-) HCA showed weight loss with no decrease in cumulative food intake. (5) It seems that the potential mechanism of weight loss with (-) HCA may include an energy expenditure component, the nature of which remains undetermined. (5) This mechanism of energy expenditure, decreased lipogenesis, and the reduction in food intake in (-) HCA-treated animals may result in loss of weight and total body fat content. (6)

Although the potential of (-)HCA as a weight lowering compound has been recognized since the 1970's, only few clinical studies have been conducted with this compound. (7-12). These few studies examining HCA-mediated prevention of excess body fat, resulted in contradictory results, most likely due to HCA being poorly bioavailable in the cytosol of a target cell. In one clinical study of HCA, a controversial high fiber diet was used. The use of a high-fiber diet in combination with HCA may reduce gastrointestinal